Q & A

Philip Ingham

Philip Ingham grew up in Liverpool and graduated from Cambridge University in 1977. He did his D.Phil in Developmental Genetics at Sussex University and postdoctoral work in Strasbourg, France before joining the laboratory of David Ish-Horowicz at the ICRF Mill Hill Laboratories. Here he applied the emerging technique of tissue in situ *hybridisation to the analysis of the* Drosophila *segmentation genes. After a short spell at the MRC Laboratory of Molecular Biology in Cambridge, he rejoined the ICRF as a Research Scientist at the Developmental Biology Unit in Oxford. His group pioneered the analysis of the Hedgehog signalling pathway in* Drosophila *and in collaboration with the labs of Andy McMahon and Cliff Tabin at Harvard University, discovered the* Hedgehog *gene family in vertebrates. In 1996 he was appointed Professor of Developmental Genetics at the University of Sheffield where he has established the Centre for Developmental Genetics.*

What turned you on to biology in the first place? Mitosis. I was in my second year at Cambridge reading Theology and Philosophy and not too sure about where this was taking me. Walking one morning through the Downing Site, where many of the science departments are situated, I decided to sit in on a lecture, which turned out to be part of a course on the biology of cells. I knew no biology at the time, having attended a traditional boys' grammar school in the north of England where biology was considered: first, not a science, and second, a subject suitable only for girls. The lecturer showed a rather grainy monochrome movie of a cell undergoing division: I was spell-bound and immediately made an appointment with my tutor to see if I could change degree courses.

What happened next? After a lot of negotiation between my tutor and the Director of Studies for natural sciences, it was decided that I could switch to Genetics, which I was informed was really a branch of mathematics masquerading as a biological science. I loved every minute of it, but especially developmental genetics: the idea that you could figure out how an organism is constructed by the application of genetic logic rather than by dissecting or grafting bits of tissue was — and still is — extremely seductive to me.

Do you have a favourite paper? My favourite papers mostly date from the late 1970s, when my interest in biology was first kindled. If I had to pick one from these it would be '*A gene complex controlling segmentation in Drosophila*' by E.B Lewis, published in *Nature* in 1978. Lewis had been working on bithorax for over twenty years, but had published remarkably little of his extensive and pioneering analyses up to that point. The distillation of the results of his many years experimentation and thought presented in this *Nature* paper was a seismic event for developmental genetics — it heralded the dawn of a new era in the analysis of *Drosophila* development, which of course was to have a major impact throughout developmental biology.

Are you pleased that you switched fields? Absolutely. I feel incredibly lucky that I unwittingly stumbled into an area of science that was on the brink of a major revolution. The opportunities for discovery were enormous and participating in this process has been exhilarating.

What is the best advice you've been given – and what advice would you offer? Michael Ashburner once told me never to do a PhD in France, which as they could take upwards of ten years to complete at the time was probably very sensible advice. I find it quite difficult to advise individuals thinking of embarking on a career in biology nowadays — the field has changed so radically over the past two decades that one's own experience hardly seems relevant to current times. Of course, the old adage about pursuing what really fascinates you remains as true today as always — but to make an original contribution I think it is more important than ever to take a multidisciplinary approach to a problem.

What has been your biggest mistake in research? My first mistake was when, as a graduate student, I isolated in excess of 2000 embryonic lethal mutations in *Drosophila* and discarded them without looking at their embryonic phenotypes! That was just about forgivable, as no one really knew what a *Drosophila* embryo looked like in those days. Aside from that, not remaining a post doc for longer is something I now regret. The desire to become independent and establish your own research group is a natural one, but the freedom of all responsibilities offered by post-doctoral research is something to be savoured for as long as possible!

What is your favourite / least favourite conference? Some of the most enjoyable conferences I have attended have been the annual BSDB Spring Symposia. But I think the 1980 EMBO *Drosophila* Workshop in Crete gave me my best and worst conference experiences. The best part was hearing Eric Wieschaus present the results of the *Drosophila* saturation mutagenesis screens that he and Christiane Nüsslien-Volhard had just completed. The worst thing was being persuaded, at the meeting, to give my first ever public research talk — unprepared and without slides! The result, needless to say, was a disaster, as was somewhat unkindly pointed out to me immediately afterwards by a certain French scientist (who will

remain nameless).

Do you have a scientific hero; if so, who and why? Several. E.B. Lewis, Eric Wieschaus, Christiane Nüsslein-Volhard and Paul Nurse all spring to mind. All are brilliant geneticists whose achievements are well known — but in addition they all share an unadulterated passion and enthusiasm for science that has inspired me and I am sure countless others.

What do you think about the publication policies of journals and the peer review system? The purpose of publishing academic research is fundamentally to disseminate knowledge. Unfortunately it has also become inextricably linked with career progression. I find the pressure to publish in 'high impact' journals regrettable for many reasons, not least of which is the disproportionate influence that a relatively small cadre of editors can exert over the progress and direction of research. The use of anonymous reviewers can reinforce this influence, while allowing unscrupulous individuals to hinder or even suppress the presentation of data for public scrutiny. But who is to blame for this? A shift in motivation from a spirit of enquiry towards an aggressive competitiveness that characterises certain cultures has fuelled the dominant position occupied by 'high impact' journals. At the same time, the massive proliferation in research activity has reinforced the importance of 'brand recognition' in the peer review system — such is the pressure on appointments and funding committees that they increasingly rely on the names of journals as guarantees of quality in lieu of scrutiny of the scientific content of the papers they publish. The whole situation is a vicious circle but one that desperately needs to be broken.

MRC Intercellular Signalling Group, Centre for Developmental Genetics, School of Medicine and Biomedical Science, University of Sheffield, Sheffield S10 2TN, UK.

Life in the fast lane

Researchers studying a species of tropical fish which exploits temporary pools that form during the African rainy season believe they may have discovered the world's shortest-lived vertebrate. Writing in the Proceedings of the Royal Society, series B, (published online), Italian scientists Stefano Valdesalici, at the Associazione Italiano Killifish in Canossa, and Alessandro Cellerino at the CNR Institute of Neuroscience in Pisa have been studying reproduction and survival of members of a captive population of *Nothobranchius furzeri*, a species selected because of the normally very limited rainy season in its natural African habit. Fishes of this genus develop rapidly, mate and lay their eggs in the muddy bottom before the water disappears. Embryos survive encased in the dry mud in a dormant state.

In the laboratory, conditions were created as close as possible to those found in temporary pools and the fish were fed freely. In as little as four weeks the largest males were developing their nuptial coloration. These were bred with females in the group and the eggs collected and stored dry. By six weeks of age, mortality amongst the adults was increasing and by 12 weeks all the adults had died. The eggs were subsequently hatched under similar conditions and this generation of fish showed similar development and survival times to their parents.

Such a lifespan is extremely short, even by comparison with other annual fish, and is more akin to *Drosophila* than other vertebrates, the authors point out.

They believe that the short lifespan is likely to be due to genetic factors and may represent the pleiotropic effects of genes that drive very fast sexual maturation, or the diversion of energy from somatic cell maintenance to growth and reproduction.

They believe that because of the features of the fish's lifestyle it may present a useful model for biologists. Enormous effort has been put into the establishment of zebrafish as a model organism, but these fish have a lifespan close to 5 years in the laboratory, they note. "Owing to its small size and the possibility of being propagated in the laboratory, maybe *N. furzeri* could become a unique animal model for ageing research," they say.

Getting a move on: Members of the species *Nothobranchius furzeri*, shown above, may be the shortest-lived vertebrates. (Photo: Dr Stefano Valdesalici.)